Decision Memo for Cardiac Pacemakers (CAG-00063R)

Decision Summary

We will maintain the current non-coverage NCD. Medicare will not cover pacemaker implantation for post-MI patients with asymptomatic bradycardia. Medicare will continue to cover pacemaker implantation for patients with symptomatic bradycardia whether iatrogenic or induced by required pharmacologic therapy.

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Decision Memo

To: Administrative File CAG-00063R

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Subject: National Coverage Determination (NCD) Reconsideration - Cardiac Pacemakers

Date: October 1, 2001

This national coverage determination (NCD) reconsideration serves four purposes: (1) references the original NCD (CAG 00063A) issued by the Centers for Medicare & Medicaid Services (CMS) (formerly known as the Health Care Financing Administration) to cover the use of a cardiac pacemaker to treat asymptomatic bradycardia in post myocardial infarction (MI) patients about to initiate long-term beta-blocker (ß-blocker) drug therapy; (2) explains the reasons why CMS decided to reconsider this NCD; (3) presents and analyzes new scientific and clinical data submitted; and (4) delineates the reasons for once again upholding the current NCD (CIM 65-6).

Initial Coverage Request

Medicare's NCD for cardiac pacemakers can be found at CIM 65-6. This NCD indicates that cardiac pacemakers are not considered reasonable and necessary for patients with asymptomatic bradycardia.

In June 2000, Medtronic requested that CMS review the use of a cardiac pacemaker to treat asymptomatic bradycardia in post-MI patients about to initiate long-term ß-blocker drug therapy. After a complete systematic review of the evidence provided, CMS posted a coverage decision memorandum on March 20, 2001, that maintained its current non-coverage NCD that pacemaker implantation would not be considered reasonable and necessary in these patients. This memorandum can be accessed at CAG-00063N. That document contains background clinical information on this topic that will not be repeated here.

Reconsideration

Medtronic Inc. (Medtronic) and Dr. Jeffery J. Goldberger of Northwestern University both requested reconsideration of the issue; we accepted these requests as a single reconsideration. A timeline of the background and recent developments/activities is listed below:

Timeline of Recent Developments and Activities

May 1985	CMS issues CIM 65-6 indicating that cardiac pacemakers are not considered reasonable and necessary for patients with asymptomatic bradycardia.
June 2000	CMS receives Medtronic's formal request for NCD that would cover cardiac pacemakers for patients with asymptomatic bradycardia.
March 20, 2001	CMS posts coverage decision memorandum CAG 00063A on the website upholding the NCD.
April 3, 2001	CMS receives Medtronic's request for reconsideration of the NCD.
April 4, 2001	CMS receives Dr. Goldberger's request for reconsideration.

April 12, 2001 Because new scientific evidence was submitted, CMS decides to reconsider this issue. The Medtronic request and Dr. Goldberger's request are combined into a single reconsideration.

April 24, 2001

CMS receives additional information from Dr. Goldberger, including the following two articles:

1. Lechat, Hulot, Escolano, et al. Heart rate and cardiac rhythm relationships with bisoprolol benefit in chronic heart failure in CIBIS II trial. Circulation. 2001: 1428-1433.
2. Rathore, Weinfurt, Gersh, et al. Treatment of patients with myocardial infarction who present with a paced rhythm. Ann Intern Med. 2001; 134: 644-651.

July 10, 2001 CMS met with Medtronic and Dr. Goldberger to discuss the reconsideration. The requestors agreed to provide CMS the following three pieces of information:

1. Additional data on how pacemaker patients tolerate ß-blockers.
2.

   Medtronic proposes that the following conditions can be used to define the asymptomatic, bradycardic post-MI population. This definition includes patients with one of the following:
   a. Resting (awake) heart rate less than or equal to 50 beats per minute on 2 consecutive days in the absence of treatment with rate-slowing medications (i.e., diltiazem, verapamil)
   b. Sinus pauses (greater than 2 seconds) during the day
   c. PR interval greater than or equal to 280 msec in the absence of medications that prolong AV nodal conduction time (digoxin, diltiazem, verapamil)
   d. Second-degree AV block, type I at rest (and awake)

   CMS requested scientific evidence to demonstrate that these conditions accurately define asymptomatic, bradycardic post-MI patients who will become symptomatic?

3.

   Provide additional information concerning the pacemaker patients in the Rathore study.

The requestor was asked to submit additional material by August 10, 2001. We therefore extended the due date of the decision memorandum to September 11, 2001 in order to review any submitted information.

August 24, 2001 CMS received additional material from Requestor.

September 13, 2001 The due date was extended to October 1, 2001.

A number of concerns about the CMS analysis were raised in the letters submitted by Medtronic and Dr. Goldberger (which we accepted as a single reconsideration). These concerns are explained in the sections below.

Summary of Evidence

The Lechat[1] study is a prospective, randomized trial designed to study the relationship between baseline heart rate, heart rate changes (at two months), nature of cardiac rhythm, and outcomes (mortality and hospitalization) in patients with congestive heart failure. The 2,647 heart failure patients were divided into three groups: those with sinus rhythm, those with atrial fibrillation, and those without sinus rhythm but with supraventricular arrhythmias other than atrial fibrillation or with pacemakers (who were excluded from the analysis). An indeterminate number of patients were post-MI; therefore, specific analysis on this population was not available. The remaining patients were randomized to bisoprolol or placebo. Heart rate was measured at baseline and during subsequent follow-up visits by pulse rate measurement or an electrocardiogram (ECG) recording. Blood pressure was also recorded. Relationships between these baseline parameters and outcomes were studied, such as mortality and hospitalization for heart failure.

Baseline values were compared to values obtained two months later. The bisoprolol dose was started at 1.25 mg and increased by 1 week steps to 2.5, 3.5, 5 mg and by 1 month steps to 7.5 and 10 mg.

There was little difference between the placebo and treatment groups for both cardiac rhythms. One difference is that the baseline heart rate was significantly lower in atrial fibrillation patients randomized to bisoprolol than those in the placebo group:

Table 1: Baseline Heart Rate

	Placebo (n=1,268)	Placebo (n=1,268)	Bisoprolol (n=1,271)	Bisoprolol (n=1,271)
	Sinus Rhythm (n=1,004)	Atrial Fibrillation (n=264)	Sinus Rhythm (n=1,014)	Atrial Fibrillation (n=257)

Heart rate, bpm	78.8(13.4)	89.7(19.2)	78.8(13.4)	85.3(17.8)

The authors found that the baseline heart rate or the extent of heart rate reduction did not influence the survival benefits from bisoprolol. Benefit was obtained for patients with sinus rhythm; however, the benefits were questionable in atrial fibrillation patients. There was no significant difference in mortality between the bisoprolol and placebo groups for atrial fibrillation patients. This study seeks to demonstrate that ß-blockade with bisoprolol improves survival regardless of an individual's baseline heart rate. Mean baseline heart rate in each study group was 78 bpm or greater, meaning that the significance of these results for bradycardic patients is unclear.

The Rathore[2] study (retrospective) involved 102,249 acute MI patients. It was designed to determine the following:

1. Proportion with paced rhythms that present with acute MI;
2. Whether patients with MI and paced rhythms are accurately diagnosed and therefore, appropriately managed; and
3. Whether mortality rates differ among patients with paced rhythms and those without.

Patients were obtained from the Cooperative Cardiovascular Project (CCP). The CCP is a data set of 234,769 Medicare beneficiaries who were treated for acute MI. The patients abstracted from this data set were further screened for this study. Study patients were confirmed to suffer from an AMI and had a documented infarction at hospital admission. A total of 132,520 patients were excluded; 102,249 were included in the study population.

The primary outcome studied was the prevalence of paced rhythms among elderly MI patients. An ECG and documentation in the patient's chart identified pacemaker patients. Of the 102,249 study patients, 1,954 or 1.9% had a pacemaker. These patients were older, predominantly male, and more likely to have had previous coronary artery bypass, MI and cerebrovascular disease compared to patients without pacemakers. Secondly, the investigators evaluated the use of aspirin, ß-blockers, and reperfusion therapy at admission for "ideal" candidates. Prescriptions of aspirin and ß-blockers at discharge were also evaluated. The following table presents a portion of the criteria used to distinguish ideal ß-blocker candidates.

Table 2: Exclusion Criteria Used to Select Ideal Cohorts for Beta-Blocker Therapies[13]

Therapy	Exclusion Criteria

ß-Blocker at admission	Pulse at admission less than 50 beats/min (unless previously taking a ß-blocker) Systolic blood pressure at admission less than 100 mm Hg Second- or third-degree heart block documented at admission Congestive heart failure at admission Previous documentation of left ventricular ejection fraction less than 0.35
ß-Blocker at discharge	Pulse at discharge less than 50 beats/min (unless previously taking a beta-blocker) Systolic blood pressure at discharge less than 100 mm Hg Second- or third-degree heart block Congestive heart failure or pulmonary edema during hospitalization

	Left ventricular ejection fraction less than 0.35

Of the 102,249 study patients, 41,088 or 40.2% were ideal candidates for ß-blockers at admission. Six hundred and three of the ideal candidates or 1.5% had pacemakers. For patients at discharge, 13,632 or 13.3% were ideal candidates for ß-blockers at discharge. Of these ideal patients, 148 or 1% had a pacemaker. Pacemaker patients were less likely than non-paced patients to receive any of the three types of acute MI therapy. Patients with pacemakers had poorer outcomes, including higher unadjusted rates of reinfarction, congestive heart failure and in-hospital mortality. The benefit that was demonstrated for patients identified and aggressively treated was apparent up to 30 days. No long-term benefit was proven.

American College of Cardiology (ACC)/American Heart Association (AHA) Recommendation

There are two sets of guidelines that are pertinent to this analysis:

1. The ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction[4]; and
2. The ACC/AHA Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices.[5]

The ACC/AHA Guidelines for the Management of Patients with Acute MI recommend that survivors of myocardial infarction be treated with long-term ß-blockers, provided that they do not have one of the following relative contraindications:

- Heart rate less than 60 beats per minute (bpm),
- Systolic arterial pressure less than 100 mm Hg,
- Moderate left ventricular failure,
- PR interval greater than 0.24 second, and
- Second- or third-degree atrioventricular (AV) block.

The guidelines further state that patients with certain relative contraindications may still benefit from ß-blockers. These contraindications are:

- Moderate left ventricular failure,
- PR interval greater than 0.24 second,

Discussions with members of the ACC/AHA group (see attachment) concerning their revised guidelines specifically stated there was no discussion about asymptomatic bradycardic patients post-MI being prophylactically paced to start ß-blockers. Further, they stated there is no evidence supporting use of ß-blockers in this population, nor is there a way of knowing if these patients will improve or what their outcome will be.

The ACC/AHA Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices are established to assist physicians in clinical decision-making. Ultimately NCDs must be based on the needs of each patient, however, this document is designed to provide general guidance. The following is a Class I recommendation with Level C evidence supporting insertion of a pacemaker:

Sinus Node dysfunction with documented symptomatic bradycardia, including frequent sinus pauses that produces symptoms. In some patients, bradycardia is iatrogenic and will occur as a consequence of essential long term drug therapy of a type and dose for which there are no acceptable alternatives.

Class I recommendations are conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful and effective. Level C evidence is a consensus opinion of experts. Medtronic interprets this recommendation to include post-MI patients with asymptomatic bradycardia who are potential candidates for long-term ß-blocker drug therapy.

The ACC/AHA guidelines do not explicitly recommend pacemaker insertion for post-MI patients with asymptomatic bradycardia who are either treated with ß-blockers or being considered for ß-blocker therapy. Whether or not ß-blockers are essential drug therapy is the central question of this review.

CMS Analysis

A key issue is trying to determine for which post-MI patients the 40% mortality benefit of ß-blockers is well established. Patients with the following relative contraindications may experience benefit: non-Q-wave infarction, older age (>80), diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure and low risk patients. We found no evidence that post-MI patients with asymptomatic bradycardia are similar to patients in these subgroups. There is no direct evidence demonstrating what benefit, if any, these patients can attain through ß-blocker treatment.

The requestor submitted the Lechat study to demonstrate that ß-blockers improve survival in post-MI patients regardless of baseline heart rate. It is important to note that these patients all had congestive heart failure and some had atrial fibrillation, which makes them different than the asymptomatic population, and it makes extrapolation even more difficult. The pharmacologic effect of ß-blockers on patients with CHF may or may not be similar to the effect of ß-blockers in post -MI patients. Extrapolating results from the Lechat study from CHF to CAD patients is probably not justified.

It may be misleading to suggest that heart rate is completely irrelevant when considering whether or not a patient will benefit from ß-blocker therapy. The mean heart rate for both the sinus rhythm and atrial fibrillation treatment and placebo groups was relatively high; in each of the four groups it was over above 77 bpm (see Table 3). Therefore, this study does not show that patients with low heart rates derive benefit from ß-blockers.

Table 3: Range of Baseline Heart Rates

	Sinus Rhythm Placebo	Sinus Rhythm Bisoprolol	Atrial Fibrillation Placebo	Atrial Fibrillation Bisoprolol
Heart rate, bpm Mean	78.8(13.4)	78.8(13.4)	89.7(19.2)	85.3(17.8)
Heart rate, bpm Range	65.4 - 92.2	65.4 - 92.2	70.5 - 108.9	67.5 - 103.1

It is necessary to highlight these numbers because the post-MI patients with asymptomatic bradycardic have much lower heart rates (less than or equal to 50 beats per minute `bpm') than the patients included in the Lechat analysis. Even if we placed greater emphasis on the study patients with lower heart rates (low end of range) it is still inaccurate to suggest that these patients are the same or similar to patients with bradycardia. A post-MI patient with a heart rate of 65 bpm is potentially much different than a post-MI patient with a heart rate of 50 bpm. This article demonstrates that individuals with a heart rate greater than or equal to 65 bpm and CHF may benefit from ß-blockers, given the range of values in Table 3, but this finding can not be inferred to all post MI patients.

ß-blocker anti-adrenergic effects have many benefits, such as preventing re-infarction, preventing arrhythmias, and improving left ventricular function. Lechat demonstrates that in a certain population there is a rate-reduction to outcome improvement relationship with ß-blockers. What has not been demonstrated is the overall benefit of ß-blockers, regardless of the mechanisms of action for the specific group in question. Lechat did not include patients that were bradycardic. Further, it may be erroneous to assume that the population studied by Lechat is similar to the post-MI, bradycardic, and asymptomatic patient in question here.

The requestor submitted the Rathore study to demonstrate that patients who are paced benefit from ß-blockers. The benefit demonstrated can not be solely attributed to the use of ß-blockers since they were not an isolated therapy. Patient's received an overall change in management including aspirin, and heparin (when appropriate) in addition to ß-blockers. Further, the benefit achieved was only present up to 30 days and no long-term benefit was proven. In general, the study showed that patients who are paced experience poor management and outcomes; we agree with the requestor that this could be attributed to the low rate of ß-blocker treatment in these patients. However, all the study participants had some indication for pacer implantation prior to the study. This clearly makes them different than the asymptomatic population in question because they experienced symptoms requiring pacemaker implantation.

It is problematic to infer data that reflects symptomatic individuals to those who are asymptomatic. For example, even though the pacemaker patients had worse outcomes, it is unknown if these outcomes are related to the underuse of aspirin, ß-blockers, or reperfusion versus a greater pre-event comorbidity (which asymptomatic patients did not experience). Secondly, the study did not seek paced patients that are having an MI and then stratify them into either ß-blocked or non-ß-blocked groups: they were retrospectively observed with no indication as to why they did or did not receive ß-blockers even when diagnosed with MI. The authors found that pacemaker patients were less likely than non-paced patients to receive any of the three standard therapies (emergent reperfusion, aspirin and ß-blockers) used to treat acute MI. This raises two questions:

1. What proportion of patients who receive pacemakers for symptomatic bradycardia then get ß-blockers post insertion?
2. If physicians have difficulty identifying MI in paced persons (demonstrated by Rathore) then are we increasing their long-term outcome risk by prophylacticaly placing them (pacers) to achieve an unquantifiable benefit (ß-blockade in this group)?

Even in "ideal" candidates there is underutilization of aspirin, ß-blockers and reperfusion therapy. This raises the question of physician bias against ß-blocking these paced patients. It is notable that exclusion criteria for ß-blocker usage included pulse at admission less than 50 bpm and 2nd or 3rd degree heart block, two of the four conditions Medtronic uses to define asymptomatically bradycardic patients. This article clearly shows there are missed treatment opportunities for MI patients without contraindications, but again fails to provide compelling evidence that we should treat those whose contraindication is a heart rate less than 50 bpm.

While the evidence to demonstrate that the targeted subset of paced patients will benefit from ß-blockers is uncertain, the risks of pacemaker use are becoming clearer. To illustrate, Maisel[6] recently published a summary of the recalls and safety alerts of pacemakers and implantable cardioverter-defibrillators (ICDs) over the last ten years, and he reported a statistically significant increase in advisory rates (advisories per 100 person-years) from 1995-2000, for both pacemakers, ICDs and total devices.

Furthermore, because some or all of the benefits found for ß-blockers may be related to decreased heart rate, it may not be valid to assume that patients who are already bradycardic will experience benefits similar to non-bradycardic patients. In fact, it is possible that pacing bradycardic patients to a higher resting heart rate would lead to an increase in mortality and morbidity that could outweigh any benefit of being treated with beta-blockers. There is no data available that would allow one to reasonably predict the clinical outcomes of these patients.

Conclusion/Decision

We will maintain the current non-coverage NCD. Medicare will not cover pacemaker implantation for post-MI patients with asymptomatic bradycardia. Medicare will continue to cover pacemaker implantation for patients with symptomatic bradycardia whether iatrogenic or induced by required pharmacologic therapy.

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1 Lechat, Hulot, Escolano, et al. Heart rate and cardiac rhythm relationships with bisoprolol benefit in chronic heart failure in CIBIS II trial. Circulation. 2001: 1428-1433.

2 Rathore, Weinfurt, Gersh, et al. Treatment of patients with myocardial infarction who present with a paced rhythm. Ann Intern Med. 2001; 134: 644-651.

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4 ACC/AHA Guidelines for Management of Patients with Acute Myocardial Infarction. Journal of American College of Cardiology. 1999; 100(9): 1016-1030.

5 ACC/AHA Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). JACC. 1998; 31(5): 1182.

6 Maisel, William H, Sweeney, Michael, O, Stevenson, William, G. Recalls and safety alerts involving pacemakers and implantable cardioverter-defibrillator generators. JAMA. 2001; 286(7): 793-799.

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